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ABSTRACT

Increasing evidence that decompensation into acute psychosis by schizophrenics can often be avoided with active pharmacological and psychosocial intervention at the early signs of relapse has stimulated research into the signs and symptoms prodromal to acute psychosis. In this study, 6-week periods prior to 17 psychotic relapses and to 11 relapses characterized by depression and/or hostility were examined for 23 recent-onset schizophrenic outpatients. These prodromal periods were compared with periods that did not precede relapse for the same patients and for 28 schizophrenic patients who did not relapse. The Brief Psychiatric Rating Scale (BPRS) and the Psychiatric Assessment Scale were used to assess symptomatology. Psychotic relapse was defined as an elevation to severe or extremely severe from non-pathological levels on one or more of the BPRS items: Hallucinations, Unusual Thought Content, and Conceptual Disorganization. Non-psychotic relapses were similarly defined using the Depression and Hostility items of the BPRS. The findings suggest that even slight elevations in delusions, hallucinations, depression, somatic concern, and guilt above the levels usually present for a given patient may presage psychotic relapse during the 6 to 8 weeks prior to its occurrence. When compared to non-prodromal periods of other patients, periods before relapse were found to show significantly higher levels of hostility and grandiosity in addition to higher levels of delusions, hallucinations, and somatic concern. For relapses characterized by depression and hostility, elevations of activation, tension, and depression were found in the prodromal period. (Author/NB)

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Prodromal Signs and Symptoms of Schizophrenic Relapse

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Abstract

Six week periods prior to 17 psychotic relapses and to 11 relapses characterized by depression and/or hostility were examined for 23 recent-onset schizophrenic outpatients. These prodromal periods were compared with periods that did not precede relapse for the same patients and for 28 schizophrenic patients who did not relapse. The Brief Psychiatric Rating Scale and the Psychiatric Assessment Scale were used to assess symptomatology. Psychotic relapse was defined as an elevation to severe or extremely severe from non-pathological levels on one or more of the BPRS items: Hallucinations, Unusual Thought Content, and Conceptual Disorganization. Non-psychotic relapses were similarly defined using the Depression and Hostility items of the BPRS. Even slight elevations in delusions, hallucinations, depression, somatic concern, and guilt above the levels usually present for a given patient may presage psychotic relapse during the six to eight weeks prior to its occurrence. When compared to non-prodromal periods of other patients, periods before relapse were found to show significantly higher levels of hostility and grandiosity in addition to higher levels of delusions, hallucinations, and somatic concern. For relapses characterized by depression and hostility, elevations of activation, tension, and depression were found in the prodromal period.

Prodromal Signs and Symptoms of Schizophrenic Relapse

Traditionally, the study of the symptoms of schizophrenia has focused on symptoms which occur in the floridly psychotic state. Only within the last two decades have the signs and symptoms prodromal to acute psychosis been systematically examined. This research has been stimulated by increasing evidence that decompensation into acute psychosis can often be avoided with active pharmacologic and psychosocial intervention at the early signs of relapse. The present study is a prospective examination of prodromal signs and symptoms of schizophrenic relapse, using a systematic and carefully controlled research design.

On the basis of an extensive literature review, Docherty, Van Kammen, Siris, and Marder (1978) have identified five stages which they believe are common to most descriptions of schizophrenic decompensation. A person in stage one, overextension, begins to feel overwhelmed. This stage is characterized by overstimulation, persisting anxiety, irritability, parapraxes, decreasing performance efficiency, and distractibility. Stage two, restricted consciousness, encompasses mental phenomena that limit the person's range of thought. Symptomatology includes boredom, apathy, social withdrawal, obsessional and phobic symptoms, somatization, hopelessness, dissatisfaction, and dependency.

The third stage, disinhibition, is a period of increased impulse expression. Risk taking, sexual promiscuity, rage attacks, and impulsive spending may occur. Ideas of reference may appear as well as dissociative phenomena and elevation of mood.

In stage four, psychotic disorganization, there is a destructuring of the external world, followed by a destructuring of the self and then total fragmentation. As the external world breaks down there is increasing perceptual and cognitive disorganization, speech production and comprehension becomes difficult, and ideas of reference are prevalent. As the person loses a sense of

self-identity, behavior is highly variable and unpredictable, a sense of connectedness disappears, primitive sexual and aggressive images intrude freely into consciousness, and severe anxiety, panic, horror, and hallucinations are present. With total fragmentation the person experiences complete loss of control. Reality testing gives way to the characteristic formal thought disorder and hallucinations of acute schizophrenic psychosis. The final stage is psychotic resolution. The panic and horror of acute psychotic disorganization decreases as delusional organization occurs.

The progression of symptomatology through these five stages is from symptoms characteristic of neurotic processes to severe psychotic disturbances. From a psychoanalytic perspective, the first two stages may be thought to represent neurotic attempts to solve a massive psychological conflict, and the latter stages represent psychotic resolution of the conflict (Donlon and Blacker, 1973; Donlon and Blacker, 1975). Chapman's (1966) conclusion was that the neurotic symptoms were part of the patient's emotional response to the illness rather than part of the underlying disease process. In either case, the descriptions of the symptomatology are the same. Theory is essential to understanding schizophrenic decompensation, but not for empirically identifying the prodromal signs.

The sequence of symptomatology described in the five stages may also be explained by a heuristic vulnerability/stress model that serves as the working model of the UCLA Mental Health Clinical Research Center for the Study of Schizophrenia (Dawson & Nuechterlein, in press; Nuechterlein & Dawson, 1984). This working model postulates the presence of enduring vulnerability characteristics such as reduced available attentional capacity to process environmental stimuli, autonomic hyperreactivity to aversive stimuli, and social competence and coping deficits. The vulnerability characteristics are assumed to be present before, during, and after schizophrenic psychotic periods and may vary in their severity from one schizophrenic patient to another. Social competence

and coping deficits are viewed as possible results of the attentional capacity limitations and autonomic reactivity abnormalities.

In this heuristic vulnerability/stress model, two major classes of stressors interact with the vulnerability characteristics-- social stressors, such as discrete life events and ongoing family stress, and a nonsupportive social network. These stressors interact with the vulnerability characteristics to create intermediate states of processing capacity overload and autonomic hyperarousal. Difficulty concentrating, persistent tension and nervousness may be manifestations of this prodromal intermediate state. When a person is in this prodromal intermediate state, a typical response to these stressors is to withdraw, which in a moderate degree may protect the patients from their worsening social environment. Withdrawal to a severe degree will lead to worsening of the social environment, which in turn continues to overload processing capacity, heighten autonomic hyperarousal, and augment defective processing of social cues. This vicious cycle is hypothesized to result in further decompensation until positive schizophrenic psychotic symptoms appear.

This heuristic vulnerability/stress model describes a process of decompensation that predicts similar symptomatology as described by the stage models. The concentration difficulties, persistent tension, and nervousness in the early states of the vulnerability/stress model correspond to the persisting anxiety and distractibility of stage one. The social withdrawal and apathy in the intermediate states of the heuristic model is described in the second stage. The vulnerability/stress model does not specify a parallel to stage three. As the cycle escalates, thinking becomes fragmented, reality is distorted, and the self-other boundary is weakened as described in stage four. As the patient decompensates further the schizophrenic psychotic symptoms of hallucinations, delusions and/or florid formal thought disorder appear, which is similar to later parts of stage four and to stage five.

None of the studies covered in Docherty et al.'s (1978) exhaustive review of the prodromal literature were prospective in design. Retrospective studies of the relapse process may involve a biased view of past events, as the negative outcome is known when data are collected. Three studies have now used prospective designs. We will comment briefly on all three. Herz, Szymanski, and Simon (1982) piloted an intermittent medication strategy for schizophrenic outpatients. The investigators gradually withdrew the medication of 19 patients who had been in relative remission for six months. Medication was resumed only when a patient experienced symptoms considered potentially prodromal to relapse. The intent of this strategy is to decrease the amount of time the patient is on neuroleptic medication by using active pharmacologic intervention only in the event of an exacerbation of symptoms. In order for this targeted medication strategy to be applied, each patient was closely monitored for the appearance of symptoms potentially prodromal to relapse. This monitoring was done in weekly group therapy sessions and assessments with the Problem Appraisal Scale and the Global Assessment Scale.

Of the 10 patients who made it through the drug washout and into the intermittent medication protocol, five experienced an increase in non-psychotic symptoms and were temporarily treated with neuroleptic medication. The symptoms typically observed were sleep disturbances, agitation, anxiety, anger, social withdrawal, and impaired social relations. It is not possible to know whether these mild elevations in symptomatology would have progressed to a full psychotic relapse. No statistical analyses were reported to indicate whether the elevations of these typical symptoms were significantly higher than for the non-relapsers.

In the context of a targeted medication protocol, Heinrichs and Carpenter (1985) examined elevations in symptomatology thought to be prodromal to schizophrenic relapse (see also Carpenter & Heinrichs, 1983, for a more detailed

description of their research protocol). In addition to 17 drug-free schizophrenic patients, a comparison group of 30 schizophrenic patients receiving maintenance neuroleptics was also included. When a decompensation was judged to have begun, the changes in signs and symptoms thought to have presaged the exacerbation were recorded. Again, prompt pharmacologic intervention prevents us from knowing whether all of these episodes of decompensation would have progressed to full psychotic relapse.

The data for the medicated and drug-free groups were combined because the groups differed on only one symptom construct, that of sleep disturbance. The ten most common prodromal symptoms in order of their frequency were hallucinations, suspiciousness, change in sleep, anxiety, cognitive inefficiency, anger/hostility, somatic symptoms or delusions, thought disorder, disruptive inappropriate behavior, and depression.

Heinrichs and Carpenter's (1985) study used a relatively unsystematic method for identification of prodromal signs, because it is analogous to the actual clinical situation. The therapist was especially watchful for the early signs and symptoms characteristic of the individual patient's previous psychotic episodes. However, because all symptoms were not examined through systematic ratings, it is difficult to know whether there were early signs other than those focused upon that may have presaged the exacerbation as well. Also, because these signs were recorded at only one point in time, subtle signs which may have appeared before the exacerbation was recognized may have gone unnoticed. Unfortunately, the non-relapsed patients were not statistically compared with the patients who relapsed.

Another recent prospective study of prodromal signs is provided by Marder, Van Putten, Mintz, Lebell, McKenzie, and Faltico (1984). Forty-one chronic schizophrenic men were followed at an outpatient clinic and treated with fluphenazine decanoate administered every two weeks. The patients were

randomized to a double-blind comparison of 5 mg or 25 mg, although both groups were combined for the analyses of prodromal signs. The Brief Psychiatric Rating Scale (BPRS) interview (Overall & Gorham, 1962) and the Symptom Checklist 90 (SCL-90) (Derogatis, 1973), a patient self-report scale, were administered at baseline, two weeks later, then monthly for three months, and then every three months. Psychotic relapse was defined as the necessity to increase medication following an increase in psychotic symptoms. Fourteen of the patients relapsed. The observations preceding the 14 relapses were compared to observations not preceding relapse within the group of relapsers as well as with observations of the non-relapsing men. Marder et al. (1984) found elevations on the thought disorder, depression, and paranoia factors of the BPRS as well as on the interpersonal sensitivity, depression, anxiety, paranoid ideation, and psychoticism factors of the SCL-90 just prior to relapse. The most discriminating factors identified by a step-wise discriminant function analysis were the paranoia and depression factors from the BPRS and the psychoticism factor from the SCL-90. There were also some indications that anxiety, depression, and interpersonal sensitivity increased earlier than did BPRS thought disorder, which is in agreement with the stage models of schizophrenic decompensation reviewed by Docherty et al. (1978).

The present study is a prospective examination of prodromal signs and symptoms of psychotic relapse among non-chronic schizophrenic patients. Assessments were made every two weeks. One clear improvement in the methodology of this study, as compared to previous studies, is that relapse was defined as the elevation of psychiatric symptoms to the severe or extremely severe level. In contrast to the previously mentioned studies, which defined relapse as the necessity to increase medication to avoid a possible relapse, we can be certain that any early symptom increases that we isolated actually were prodromal to

relapse. In addition, we were able to follow the course of the prodrome, from early signs all the way to relapse.

The present study also employed comparisons similar to those of Marder et al. (1984). The six-week period prior to the relapse period was compared to a six-week period not preceding a relapse for the relapsing patients (within-patients comparison). In addition, the prodromal periods were compared to six-week periods of symptomatology in patients who did not relapse (between-patients comparison). These two comparisons provide the best controls possible for our purpose. The within-patient comparison addresses the question of whether any specific symptoms become elevated, prior to relapse, over and above the levels usually present for these same patients. The between-patients comparison examines whether any symptoms occur at higher levels, during the prodromal periods, than those usually found among non-relapsing patients.

This study also examined non-psychotic relapses in schizophrenic patients, namely relapses involving either severe depression or hostility. Examination of these relapses was useful in determining whether some prodromal signs preceded psychotic relapse, as opposed to other types of relapse. See Figure 1 for a summary of this research design.

The present study focused on a non-chronic population, whereas the previous prospective studies have used older and more chronic patients. Recent-onset patients have advantages for the examination of prodromal signs as their course is less stable. This variability allows for distinct periods of remission followed by exacerbation of symptoms prodromal to relapse.

Like the Marder et al. (1984) study, we used the BPRS to examine symptomatology. This instrument was created specifically to measure patient change. High levels of reliability and validity have been established for the BPRS in many previous studies (Hedlund & Vieweg, 1980). Interrater reliability had also been established among the interviewers for the project within which the

present study was completed. BPRS ratings were made every two weeks, which allowed greater sensitivity for detecting prodromal signs than the less frequent administration of Marder et al. (1984).

The major focus of this study was on relapse of florid positive symptoms of schizophrenia. Negative symptoms of schizophrenia have been hypothesized to be a separate symptom dimension that is associated with a more chronic course and possibly with a structural brain abnormality (Crow, 1980, 1985). This investigation afforded us the opportunity to evaluate whether negative symptoms were predictive of episodes of acute positive schizophrenic symptoms. Likewise, the role of negative symptoms in relapse characterized by depression and hostility was evaluated. Finally, the effects of neuroleptic medication on both positive and negative prodromal symptoms was examined.

Method

Subjects

Fifty-one schizophrenic patients who attended the UCLA Aftercare Clinic served as subjects. Twenty-three patients relapsed a total of 28 times. Seventeen of the 28 relapses were psychotic and the other 11 were non-psychotic relapses (extreme depression or hostility), with 5 patients having both a psychotic relapse and a non-psychotic relapse on separate occasions. Another 28 subjects were non-relapsed comparison patients.

The 51 schizophrenic subjects are participants in a larger longitudinal follow-through study of the early phase of schizophrenic disorders, entitled Developmental Processes in Schizophrenic Disorders (Principal Investigator: Keith H. Nuechterlein, Ph.D.) being conducted at the Aftercare Clinic of the UCLA Neuropsychiatric Institute (please see Nuechterlein, Edell, Norris, and Dawson, 1986, for a complete description of the subject sources). These subjects were required to have: 1) a diagnosis of schizophrenia or schizoaffective disorder, mainly schizophrenic, by Research Diagnostic Criteria (RDC) (Spitzer, Endicott, &

Robins, 1978), based on an expanded version of the Present State Examination administered to the patient and consideration of any additional data gathered from relatives; 2) a major psychosis lasting at least two weeks with the first episode occurring not longer than two years before project contact; 3) age between 16 and 45 years; and 4) a Caucasian or acculturated Asian or Hispanic background. Subjects with any of the following were excluded: 1) evidence of an organic central nervous system disorder (e.g., epilepsy); 2) significant and habitual drug or alcohol abuse in the six months prior to project intake, or clouding of the diagnostic picture by past drug or alcohol abuse; or 3) premorbid IQ less than 70.

Of the 51 patients, 40 were men and 11 were women. Forty-two of the patients were given diagnoses of schizophrenia and the other nine diagnosed as schizo-affective, mainly schizophrenic, using RDC criteria at project entry. Forty-six patients were Caucasian, 4 were Hispanic, and 1 was of mixed heritage. The patients were relatively young (mean age at study entry = 23.5 years; S.D. = 3.5; range 18 to 32 years) and had only recently become ill (mean total time ill prior to admission to the clinic, including prodromal symptoms = 13.3 months; S.D. = 11.6; range 1 to 48 months). The patients had completed an average of 12.2 years of school (S.D. = 2.3; range 5 to 16 years). Mean social class level, as measured by the Amherst modification of Hollingshead's (1957) Two-Factor Index of Social Position was 3.1 (S.D. = 1.3, range 1 to 5). There were no statistically significant differences on the RDC diagnostic subtypes or on any of the demographic variables between the psychotic relapsers and their comparison patients, or between the non-psychotic relapsers and their comparison patients.

Seven of the psychotic relapsers were on standardized maintenance neuroleptics (12.5 mg. fluphenazine decanoate, one shot every 2 weeks) as part a research protocol, 6 were off medication completely, and 4 were on some combination of fluphenazine decanoate and/or another medication (e.g.,

antidepressants) at time of relapse. During the periods used as within-patient comparison periods, seven of the psychotic relapsers were on maintenance neuroleptics, 5 were off medication completely, and 5 were on some combination of medications. Twelve of the non-relapsed comparison patients were on maintenance neuroleptics, 2 were drug-free, and 3 were on a combination of medications.

Seven of the relapses characterized by depression and/or hostility occurred while the patient was on maintenance neuroleptics, 1 during a drug-free period, and 3 during a period in which a combination of medications was being administered. During their own comparison periods, six of the non-psychotic relapsers were on maintenance neuroleptics, 1 was off medication completely, and 4 were on some combination of medications. Eight of the comparison patients were on maintenance neuroleptics, 1 was drug-free, and 2 were on a combination of medications. The patients who were drug-free were in a drug withdrawal phase of the clinic research protocol, which was offered to patients who showed reasonable clinical stability during their first outpatient year on maintenance neuroleptics.

Procedure

The Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962) and the Psychiatric Assessment Scale (PAS) (Krawiecka, Goldberg, & Vaughn, 1977) were rated following a clinical interview intended for this purpose, which was administered every other week as part of the patients' meeting with their case managers. The BPRS consists of 18 relatively independent psychiatric symptom constructs which are rated on the basis of this brief interview. Each item is rated on a 7-point scale, using a BPRS version with clearly specified criteria for each item (Lukoff, Nuechterlein, & Ventura, 1986, in Lukoff, Liberman, & Nuechterlein, 1986). Thus, this assessment instrument is particularly suited for measuring patient change. Five factors--Thought Disturbance, Anergia, Anxiety-Depression, Hostile-Suspiciousness, and Activation--have been derived

from these eighteen items by Guy (1976) to examine separate symptom dimensions. The mean of the 18 individual items was used as a measure of overall symptomatology. The PAS consists of eight items, each rated on a 5-point scale on the basis of this same interview. It includes seven of the BPRS constructs in addition to poverty of speech.

Psychotic relapse was defined as a rating of 6 or 7 (severe or extremely severe) on the Unusual Thought Content, Hallucinations, or Conceptual Disorganization items of the BPRS. Non-psychotic relapse was defined as a rating of 6 or 7 (severe or extremely severe) on the BPRS items of Depression or Hostility. For our purposes, relapses were not included if they followed a prior relapse without a return to a moderate level (4 or below) for at least three months. If a patient relapsed more than once while he or she attended the clinic, we selected the prodromal period with the most regular data points (once every two weeks) and if possible, one during which the patient was on standardized protocol medication.

For each patient who relapsed, a period not preceding relapse was identified for use as a within-patient comparison. If an appropriate comparison period was not available, the patient was not included in the study. To discriminate these periods from relapse periods, a six-week period was chosen which contained no ratings of 5 or above on any of the five relapse scales and for which a 5 did not occur on any relapse scale for at least two following months. Again, if more than one period was available, the period with the most regular data points was used. If periods longer than six weeks occurred, the first and then the last months were dropped so as to cut the length of the period to six weeks. In the case of more than one appropriate comparison period with regular data points, the period during which medications were most similar in type and dosage to that of the prodrome was used. If at this point two or more comparison periods were equivalent in all other respects, we selected the comparison period which helped

equate the ratio between comparison periods that follow the prodrome and those which precede the prodrome.

The between-patient comparison periods were obtained from patients who had not relapsed. The period was identified in the same manner as the within-patient comparison. Seventeen periods from the non-relapsing patients were selected for comparison to the 17 psychotic relapsers and another 11 comparison periods were selected for comparison to the non-psychotic relapsers. An attempt was made to equate the relapse and control groups with respect to type and dosage of medications and time since admission to the clinic. The distribution of medication status did not differ significantly across relapse and comparison groups. Neither were there statistically significant differences in time since admission to the clinic (at the time of relapse or, for nonrelapsers, the end of the comparison period) between the psychotic relapsers and their comparison patient group or between the non-psychotic relapsers and their comparison patient group.

Results

Statistical Approach

In order to avoid excessive Type I error, the following strategy was implemented for the data analyses. The BPRS mean psychopathology score and the five BPRS factor scores (Guy, 1976) were examined initially to evaluate differences between prodromal and comparison periods. The BPRS items that load on a factor were examined only if the factor score showed significant discrimination. Individual BPRS items that defined each type of relapse were also examined as possible predictors of that type of relapse. *F* tests with conservative degrees of freedom were used to evaluate all repeated-measure effects following Greenhouse-Geisser (Winer, 1971).

Although a conventional test of statistical significance does not apply in the comparison of groups formed on the basis of the dependent variables, *t* tests

were computed at the relapse point for each of the five BPRS scales used to define relapse simply to illustrate the degree of separation created by the group-defining criteria.

Psychotic Relapse

Seventeen psychotic relapses were examined, 8 of which were relapses on BPRS Unusual Thought Content, 3 on BPRS Hallucinations, and 6 on both Unusual Thought Content and Hallucinations. No BPRS Conceptual Disorganization relapses met the full inclusion criterion and thus none were used.

Within-Patient Comparison. A t test was computed for each of the five BPRS items used as relapse criteria between the relapse point (weeks 0 to 2) and the corresponding point (weeks 0 to 2) for the within-patient comparisons. The relapse and comparison points were successfully distinguished by the defining criteria as evidenced by differences on both Hallucinations (Ms = 4.06 and 1.11, respectively), $t(16) = 5.18$, $p < .0001$, and Unusual Thought Content (Ms = 5.53 and 1.53), $t(16) = 10.55$, $p < .0001$. Depression also distinguished the two points (Ms = 3.53 and 1.70), $t(16) = 5.04$, $p < .0001$. There was a non-significant tendency for the relapse and comparison points to differ on Conceptual Disorganization (Ms = 1.82 and 1.10), $t(16) = 2.06$, $p < .06$.

To examine prodromal symptoms, ANOVAs were computed for the BPRS mean psychopathology score and for each of the five BPRS factors derived by Guy (1976). Week (6-8, 4-6, and 2-4 weeks prior to the end of the 0-2 week block) and period (prodrome, comparison) were examined as repeated-measure variables in 3 x 2 ANOVAs. This constituted the within-patient comparison. The overall symptomatology level (BPRS mean psychopathology score period effect, $F(1, 16) = 7.68$, $p < .02$) was higher for the patients during the six weeks prior to relapse than during the periods which had not preceded a relapse. See Table 1 for means and standard deviations for this effect and all other significant period effects for psychotic relapses. The most salient contributions to the overall

symptomatology level increase, during the prodromal periods, were elevations of the BPRS Anxiety-Depression factor, $F(1, 16) = 12.74$, $p < .003$, and the BPRS Thought Disturbance factor, $F(1, 16) = 8.97$, $p < .009$. A non-significant tendency for the Hostile-Suspiciousness factor, $F(1, 16) = 3.83$, $p < .07$, to be elevated was also present. In addition to these period effects, there was a week effect for the BPRS Thought Disturbance factor, $F(1.52, 24.31) = 5.28$, $p < .02$, which reflected an increase in thought disorder during weeks 2 to 4 of both the prodrome and the comparison period.

Insert Table 1 about here

ANOVAs were computed for each of the individual BPRS items which constituted the Anxiety-Depression and Thought Disturbance factor scores, in order to determine the items which made significant contributions to the separation of prodromal and within-patient comparison periods. The BPRS Anxiety-Depression factor items of Depression, Guilt, and Somatic Concern were significantly elevated prior to relapse as compared to periods not prodromal to relapse for the same patients (please see Table 2 for F ratios and significance levels of the period effects for the individual BPRS items for the psychotic prodromes). The fourth Anxiety-Depression factor item, BPRS Anxiety, was not significantly elevated.

Insert Table 2 about here

The items contributing to the BPRS Thought Disturbance factor which were elevated to a statistically significant level during the prodrome as compared with the control period were Unusual Thought Content and Hallucinations. As noted earlier, these were also the psychotic relapse criterion items on which

relapses occurred. There was also a non-significant tendency for a Period x Week interaction effect for Unusual Thought Content, $F(1.53, 24.44) = 3.61$, $p < .06$, which reflected a drop during weeks 4 to 6 of the prodrome followed by a moderate increase in unusual thinking during weeks 2 to 4. The elevations of the other two items contributing to the BPRS Thought Disturbance factor, Grandiosity and Conceptual Disorganization, were not statistically significant.

Between-Patient Comparison. The between-patient comparison was used to determine whether the within-patient prodromal findings would generalize to differences between patients who relapsed and those who did not relapse. A t test was computed for each of the five BPRS items used as relapse criteria between the relapse points (weeks 0 to 2) for the 17 relapsing patients and the corresponding points (weeks 0 to 2) of the comparison periods for the 17 non-relapsers. The defining criteria for relapse and nonrelapse points led to differences in Unusual Thought Content (Ms = 5.53 and 1.12, respectively), $t(32) = 13.28$, $p < .0001$; Hallucinations (Ms = 4.06 and 1.18), $t(17.6) = 4.97$, $p < .0001$; and Conceptual Disorganization (Ms = 1.82 and 1.00), $t(16.0) = 2.31$, $p < .04$. In addition, both Depression (Ms = 3.53 and 1.53, respectively), $t(26.6) = 4.95$, $p < .0001$ and Hostility (Ms = 1.94 and 1.18), $t(23.9) = 2.73$, $p < .02$, showed significant differences.

To examine prodromal symptoms, ANOVAs were computed for the the BPRS mean psychopathology score, and for the five BPRS factor scores, with week (6-8, 4-6, and 2-4 weeks prior to the end of the 0-2 week block) as a repeated measure and period (prodrome, comparison) as a between-patient variable. This constituted the between-patient comparison. The overall symptomatology level was elevated significantly higher prior to psychotic relapse than during the comparison period (BPRS mean psychopathology score period effect, $F(1, 32) = 4.83$, $p < .04$). See Table 1 for the means and standard deviations for significant period effects in this section. The two BPRS factors which contributed to this overall rise in

symptomatology were Thought Disturbance (period effect, $F(1, 32) = 12.01$, $p < .002$; Period x Week interaction, $F(1.46, 46.99) = 5.54$, $p < .02$) and Hostile-Suspiciousness (period effect, $F(1, 32) = 7.44$, $p < .02$). The Thought Disturbance and Hostile-Suspiciousness period effects represented elevations during the prodromes as compared to the control period. The Thought Disturbance interaction effect reflected a slight decrease in this symptom during weeks 4 to 6 and a small rise during weeks 2 to 4 in the prodromal period relative to the comparison period.

ANOVAs were computed for the individual BPRS items which constitute the above BPRS factor scores. Three of the four items contributing to the Thought Disturbance factor, namely Unusual Thought Content, Hallucinations, and Grandiosity, had statistically significant elevations during the prodromes. For Unusual Thought Content there was also a Period x Week interaction, $F(1.46, 46.71) = 4.72$, $p < .03$, which reflected a slight decrease at 4 to 6 weeks followed by a moderate increase at 2 to 4 weeks in the prodromal period relative to the comparison period. For the BPRS Hostile-Suspiciousness factor, the Hostility item was significantly elevated (period effect) and the Suspiciousness item showed a nonsignificant tendency to be elevated (period effect). The other item for that factor, Uncooperativeness, did not show a significant elevation.

Thus far in the analysis, it appears that delusions and hallucinations are common to both the within-patient and between-patient analyses, and elevations in hostility, suspiciousness, and grandiosity occur only for the between-patient comparison. However, ANOVAs were not computed for the BPRS items of Hostility and Suspiciousness for the between-patient analysis, because the period effect for the factor on which they load, Hostile-Suspiciousness, was not statistically significant. In order to verify that these symptoms were elevated only for the between-patient comparison, ANOVAs were computed for these two items for the within-patient comparison in the same manner as before. No significant effects

were found. In a similar manner, to confirm that elevations in somatic concern, depression, and guilt occurred only for the within-patient analysis, ANOVAs were computed for these items for the between-patient comparison. A significant elevation in the BPRS Somatic Concern score was found (period effect). Thus, a direct examination of individual BPRS item differences suggests that between-patient differences in somatic concern parallel those for the within-patient analysis slightly more than was initially apparent. Although computing these five additional ANOVAs increased the risk of Type I error, these comparisons were important to clarify the extent to which these prodromal symptoms were specific to within-patient versus between-patient comparisons.

Discriminant Analysis of Psychotic Relapses. A discriminant analysis was computed using all five BPRS factor scores during the period six to eight weeks prior to relapse to determine if relapse can be distinguished from comparison periods of non-relapsing patients on the basis of symptomatology which occurs well in advance of the actual relapse. A stepwise procedure was employed with F-to-enter set at 2.1 and F-to-remove set at 2.0. Two factors contributed to the discrimination, BPRS Hostile-Suspiciousness, $F(1, 31) = 3.66$, and BPRS Thought Disturbance, $F(1, 31) = 2.16$. The overall predictive model was significant, $F(2, 31) = 3.91$, $p < .05$. This model correctly classified 10 of the 17 relapses (58.8%) and 15 of the 17 comparison periods (88.2%) for a total correct classifications rate of 73.5%. The Lachenenbruch and Mickey (1968) jackknife procedure reduced correct classifications only slightly (70.6%). Classification of relapse periods continued to be correct for 58.8% of the cases. However, classification of control periods fell slightly to 82.4%.

Medication Versus Drug-Free Comparison. In order to determine if there were any differences during the psychotic prodromes between the 7 patients who were on protocol medication and the 6 patients who were off medications, ANOVAs were computed for the BPRS mean psychopathology score, and for each of the five BPRS

factor scores. Medication (on protocol medication, off medication) was entered as a between-group factor and week (6-8, 4-6, and 2-4 weeks prior to the end of the 0-2 week block) as a repeated measure. No significant effects were found. The power to detect differences for this test was low due to the small number of patients involved, so larger sample sizes will be necessary to examine this issue more fully.

Differences Between Comparison Groups. To determine if the within-patient and between-patient comparison periods were significantly different from each other, ANOVAs were computed for each of the five BPRS factors with comparison period (within, between) as a between-group variable and week (6-8, 4-6, and 2-4 weeks prior to the end of the 0-2 week block) as a repeated measure variable. In general, no significant differences were found. One Period x Week interaction effect occurred for the Thought Disturbance factor ($F(1.7, 54.8) = 4.74$, $p < .02$), reflecting extremely small initial changes in values, in opposite directions, which had no apparent effect on the interpretation of the interaction effect for this factor for the contrast between the prodromal period and the between-patient comparison period. ANOVAs were computed for the four individual BPRS items which constitute the Thought Disturbance factor. No significant effects were found.

Depression and Hostility Relapses

Eleven relapses were examined: 7 relapses on the BPRS Depression scale, 3 relapses on the Hostility scale, and 1 relapse on both Depression and Hostility.

Within-Patient Comparison. A t test was computed for each of the five BPRS items used as relapse criteria between the relapse points (weeks 0 to 2) and the corresponding points (weeks 0 to 2) for the within-patient comparison periods. The relapse and comparison points were successfully discriminated by the defining criteria, as shown by differences on Depression (Ms = 4.82 and 1.64, respectively), $t(10) = 5.30$, $p < .001$, and similar tendencies on Hostility (Ms =

3.36 and 1.64), $t(10) = 2.16$, $p < .06$. The relapse point was also characterized by more Unusual Thought Content than the comparison point (Ms = 2.55 and 1.45), $t(10) = 2.50$, $p < .04$, and a nonsignificant tendency toward more Hallucinations (Ms = 2.27 and 1.27), $t(10) = 1.91$, $p < .09$. Thus, although these relapses were characterized by predominance of severe depression or hostility, some increase in psychotic symptoms is also suggested.

To examine prodromal symptoms, ANOVAs were computed for the the BPRS mean psychopathology score, and for the five BPRS factor scores, with week (6-8, 4-6, and 2-4 weeks prior to the end of the 0-2 week block) and period (prodrome, comparison) as repeated measure factors. This constituted the within-patient comparison. Effects for the mean psychopathology score were not significant. The BPRS Activation factor score, $F(1, 10) = 5.64$, $p < .04$, was elevated during the prodrome as compared with the control period. Means and standard deviations for this and other significant period effects for non-psychotic relapses are presented in Table 3. A non-significant tendency for a decrease in the BPRS Anergia factor (period effect, $F(1, 10) = 4.56$, $p < .06$) was also noted. A week effect occurred for the BPRS Anxiety-Depression factor, $F(1.77, 17.72) = 3.74$, $p < .05$, which reflected a general increase on this symptom dimension over the course of both the prodrome and the comparison period.

Insert Table 3 about here

None of the individual BPRS items which load on the BPRS Activation factor (Excitement, Tension, Mannerisms and Posturing) were significantly elevated, although there was a non-significant tendency for Tension to be elevated (period effect). See the bottom section of Table 2 for F ratios and significance levels of the period effects for the individual BPRS items for the non-psychotic prodromes. Additional ANOVAs were computed for the Hostility and Depression

items as these were the relapse criteria items. The elevation of hostility during the prodromes as compared to the control periods was not statistically significant. The BPRS Depression item tended to be elevated (period effect) during the prodromal period, although this elevation was not statistically significant. A statistically significant week effect, $F(1.73, 17.31) = 12.81$, $p < .001$, for the same item reflected a general increase in depression over the course of both the prodromes and the comparison periods.

Between-Patient Comparison. The following between-patient comparisons were made in order to determine whether the within-patient prodromal findings would generalize to comparisons with patients who had not relapsed. A t test was computed for each of the five BPRS items used as relapse criteria between the relapse points (weeks 0 to 2) for the 11 relapsing patients and the corresponding points (weeks 0 to 2) of the comparison periods for the 11 non-relapsers. The two points that were defined by the relapse criteria differed on both Depression (Ms = 4.82 and 1.73, respectively), $t(20) = 4.42$, $p < .001$, and Hostility (Ms = 3.36 and 1.27), $t(11.5) = 2.81$, $p < .02$. In addition, there was a nonsignificant tendency for these points to differ on Hallucinations (Ms = 2.27 and 1.09), $t(10.6) = 2.15$, $p < .06$.

To examine prodromal symptoms, ANOVAs were computed for the BPRS mean psychopathology score, and for each of the 5 BPRS factor scores, with week (6-8, 4-6, and 2-4 weeks prior to the end of the 0-2 week block) as a repeated measure and period (prodrome, comparison) as a between-patient variable. No significant effects were observed for the mean psychopathology score. A statistically significant general elevation of the BPRS Activation factor score, $F(1, 20) = 6.43$, $p < .02$, during the prodromal period was present. There was also a nonsignificant tendency toward an elevation of the BPRS Hostile-Suspiciousness factor, $F(1, 20) = 3.32$, $p < .09$, during the prodrome.

Additional ANOVAs were computed for the three BPRS items which made up the Activation factor score. The only statistically significant effect for individual items included in the Activation factor score was a period effect for BPRS Tension. Interestingly, the elevation in tension tended to decrease in magnitude over the course of the prodrome, which resulted in a non-significant tendency for a Period x Week interaction effect, $F(1.27, 25.38) = 3.20$, $p < .08$.

Additional ANOVAs were computed for BPRS Hostility and BPRS Depression, as these were the relapse criteria. Hostility was somewhat elevated during the prodromes (period effect), but not significantly so. Week and Period x Week interaction effects occurred for BPRS Depression (week effect, $F(1.95, 39.01) = 5.44$, $p < .009$; Period x Week effect, $F(1.95, 39.01) = 4.03$, $p < .03$). These effects reflected increasing levels of depression over successive weeks of both periods, with this elevation occurring particularly more strikingly during weeks 2 to 4 of the prodromal period.

The results for the PAS items verified and confirmed the BPRS findings. In order to conserve space, the PAS results are not detailed.

Discussion

The major finding of this study is that there are identifiable early signs of psychotic and of non-psychotic relapses for schizophrenic patients.

Overall symptomatology was increased during the psychotic prodromes in comparison with periods that did not precede relapse for the same patients (within-patient comparison). These elevations occurred mostly for the symptoms which load on the Thought Disturbance and Anxiety-Depression factors of the BPRS. Delusions and hallucinations were significantly elevated during the prodrome preceding psychotic relapse. Also significantly elevated during the prodrome were symptoms measured by the BPRS items of Depression, Somatic Concern, and Guilt. Thus, a combination of lower-level psychotic and non-psychotic

symptoms presaged relapses that were characterized by very severe psychotic symptoms.

A somewhat different set of signs prodromal to psychotic relapse became apparent in comparison with patients who did not relapse (between-patient comparison). Delusions, hallucinations, and somatic concern still preceded relapse. However, depression and guilt were no longer significantly elevated in the prodromal period relative to the comparison period. Thus, these last two symptoms are increased in the pre-relapse period relative to the levels existing during non-relapsing periods of the same patients, but are not significantly higher that the levels shown by schizophrenic patients who did not relapse.

In the between-patient analysis, in addition to elevations in delusions, hallucinations, and somatic concern prior to relapse, there were increases in BPRS Hostility and BPRS Grandiosity. The BPRS Suspiciousness scale showed a tendency to be elevated, but this difference did not reach statistical significance. These three symptom constructs are not psychotic symptoms per se. However, they accompany paranoia and probably occur here because about two-thirds of the schizophrenics in this sample were of the paranoid subtype. These symptoms were not elevated in the within-patient comparison.

The delusions which occurred during the prodromal period of the schizophrenic relapses became much more prominent during the period two to four weeks prior to the relapse point. This is concordant with Marder et al.'s (1984) finding that worsening on the BPRS Thought Disorder factor occurred only within four weeks of relapse. There was no evidence that any of the other symptoms peaked at specific times during the course of the prodrome as would be predicted by the stage models of schizophrenic decompensation reviewed by Docherty et al. (1978). However, this is only a test of a specific version of the stage models, one in which the timing of the stages is relatively uniform across all patients and occurs over a six to eight week period. Patients may vary greatly in the

time taken to progress through the five stages, thereby leading to symptom sequences going undetected in the group averages examined in the present study.

The stage models reviewed by Docherty et al. (1978) and the vulnerability/stress model of Nuechterlein and Dawson (1984) also predict the presence of non-schizophrenic symptoms in the early prodromal period before schizophrenic relapse. The Anxiety-Depression factor of the BPRS was significantly elevated in the prodromal period relative to the control period for the same patients. This difference was evident during the prodromal periods in the individual ratings of depression, guilt, and somatic concern, symptoms characteristic of the hypothesized non-psychotic early stages. Irritability, as measured by the BPRS Hostility item, was also found in the prodromes as predicted. A few additional prodromal symptoms predicted by these models are not measured by the BPRS, and therefore, could not be examined. This study did not confirm the presence of elevated tension and anxiety.

The results of this study are in partial agreement with the three previous empirical prospective studies of schizophrenic decompensation (Herz et al., 1982; Heinrichs & Carpenter, 1985; Marder et al., 1984). Increases in hostility and suspiciousness were found in the psychotic prodromes, as reported by all three earlier studies. In addition, anxious depression and thought disturbance were significantly elevated, as reported in the two latter studies which included adequate non-relapsing controls. The present findings did not confirm the presence of anxiety and tension as found in these previous studies. Although the BPRS Anxiety-Depression factor was significantly elevated for the within-patient comparison, the individual BPRS Anxiety item was not significantly elevated, nor was the BPRS Tension item. Only one of these three previous studies (Marder et al., 1984) employed psychotic exacerbation as the relapse definition, the other two defined relapse as the appearance of symptoms judged to be prodromal to a schizophrenic episode. Thus, many of the symptom exacerbations in the Herz et

al. (1982) and Heinrichs and Carpenter (1985) studies may not have proceeded to psychotic relapse as defined here. Perhaps anxiety and tension are more characteristic of general exacerbation among schizophrenic patients, and are not prodromal to psychotic relapse. Change in sleep, which was reported in two of the earlier prospective studies (Herz et al., 1982; Heinrichs & Carpenter, 1985), was not measured in the present study.

The mean elevations in the prodromal symptoms reported in this study are small, on the order of one-half to one point on a seven-point scale. An inspection of the raw data revealed that typical elevations were slightly larger. For three patients, the periods preceding psychotic relapse had virtually no prodromal symptoms evident in the BPRS factor scores. Several additional patients did not begin to decompensate until two to four weeks prior to the relapse. Thus, these patients lowered the magnitude of the mean elevations during the psychotic prodromal periods. However, the typical elevations during the identifiable individual prodromal periods were also relatively small and imply that schizophrenic patients should be closely monitored for even small changes in symptomatology, especially for changes in the early signs and symptoms reported here. In order to identify prodromal periods, one would need to detect small increases in delusions, hallucinations, somatic concern, depression, and guilt relative to the patient's usual levels, and would also need to be alert for the presence of hostility, suspiciousness and grandiosity, even at low levels. Regular assessment on systematic rating scales such as the BPRS facilitates such monitoring (Lukoff, Liberman, & Nuechterlein, 1986).

The findings of the present study, taken together with those of the previous empirical prospective studies of schizophrenic relapse, indicate that it is often possible to identify signs of impending relapse early enough to attempt to abort the same with a pharmacologic intervention. This identification of early

prodromal symptoms is necessary for the targeted medication strategy to be feasible.

Another method that has been used to monitor schizophrenic patients is to create a checklist of the symptoms that were characteristic of the individual patient's previous prodromes, and to then monitor these specific symptoms closely (Falloon, Boyd, McGill, Razani, Moss, & Gilderman, 1982; Heinrichs & Carpenter, 1985). Validation of this method would require the examination of more than one prodrome per patient. Although this approach may be a valuable adjunct or alternative to the strategy examined here, finding idiosyncratic prodromal signs was not the focus of this study.

In order to determine if relapse could be predicted as early as six to eight weeks prior to its occurrence, the five BPRS factor scores from that period were entered into a discriminant analysis of the psychotic prodromes and the corresponding comparison periods of the non-relapsing patients. The Hostile-Suspiciousness and Thought Disturbance factors contributed to the best discrimination of relapse and non-relapse periods. Of the relapse prodromes, 58.8% (10 of 17) were correctly classified, as were 88.2% (15 of 17) of the comparison periods. This discrimination was specific, but not sensitive. We noticed that one could obtain the same hit rate by using simple integer approximations of the actual weights used by the computer program. The use of a cutting score of four or more on the formula, one times the Thought Disturbance factor score plus two times the Hostile-Suspiciousness factor score, resulted in the same classification rates as above. A cutting score of 3.5 or more allowed increased sensitivity to 82.4% (14 of 17) of the relapse prodromes, but at the cost of incorrectly classifying 7 of the 17 comparison periods as relapse prodromes (58.8% correct). Thus, one would need to consider the relative costs and benefits of using the lower cutting score in any application of this formula.

To generate a simple within-patient decision rule that could be evaluated in

subsequent research, we examined the week-to-week changes in the three factors that were significantly elevated in the prodromal period relative to the within-patient comparison period. Twelve of the 17 psychotic relapses (70.6% sensitivity) were preceded by an increase of any size in the Thought Disturbance factor score for the BPRS covering the two to four week period prior to the relapse. A similar increase in this factor occurred in only 2 of the 17 within-patient control periods (88.2% specificity). The overall classification rate was 79.4%. Thus, in this sample, any increase in the BPRS Thought Disturbance factor is highly predictive of a psychotic relapse within the next four weeks. Further research with other, and larger, samples is necessary to evaluate the validity of this decision rule.

No significant differences were found in the psychotic prodromes between medicated and drug-free patients. To fully test for the effect of medication a larger sample would be necessary.

The findings for the depression and hostility relapses were similar for both the within-patient and between-patient comparisons. Only one of the five BPRS factors, Activation, was significantly elevated during the prodromes, and this occurred relative to each type of comparison. Of the individual symptom constructs loading on the Activation factor, only tension for the between-patient comparison was significantly elevated. It is interesting that depression was not significantly elevated during these prodromal periods, although the differences were in this direction. Even though Hostility was a relapse criteria scale, there was only a non-significant tendency for the Hostile-Suspiciousness factor and for the individual BPRS item of Hostility to be elevated during the prodrome. These tendencies for increased levels of hostility occurred only when the prodromes were compared to periods for non-relapsed patients. The absence of any statistically significant effects for hostility may be due, in part, to the small proportion (4 of 11) of hostility relapses or, alternatively, these

relapses may have represented impulsive acts of aggression with no foreshadowing. It may be noteworthy that increases in hostility were statistically significant for the psychotic prodromes but not for the non-psychotic prodromes. Also of interest is the finding that increases in depression without concurrent increases in hallucinations, delusions, somatic concern, and guilt tend to predict non-psychotic relapse, not psychotic relapse.

Negative symptoms such as blunted affect were conspicuously absent from both the psychotic and non-psychotic prodromes. This finding is in concordance with Crow's (1985) suggestion that negative symptoms are part of a separate dimension of pathology than that of positive schizophrenic symptoms. Use of a rating scale that more fully examines negative symptoms would be necessary to confirm these findings, however.

In conclusion, we have found that appearance or worsening of delusions, hallucinations, depression, somatic concern, or guilt precede full psychotic relapse among schizophrenic patients by as long as six to eight weeks. Even mild elevations in these symptoms above the levels usually present for a given patient may portend psychotic relapse. At six to eight weeks prior to psychotic relapse, the presence of increased hostile-suspiciousness and thought disturbance were the most powerful predictors. Compared to schizophrenic patients who did not relapse, relapsing patients were also characterized by significantly higher levels of hostility and grandiosity in the prodromal period.

For nonpsychotic relapses in schizophrenic patients that involve severe depression or hostility, elevations of activation and tension are found in the prodromal periods. Thus, not only are prodromal symptoms apparent as long as six to eight weeks before relapse, but symptoms preceding non-psychotic relapses involve increases in activation and tension, whereas these symptoms are not significant parts of the prodrome of psychotic relapses.

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Table 1

Mean BPRS Scores for Psychotic Prodromes and Comparison Periods

	Six-Week Periods		
		Within-Patient	Between-Patient
BPRS Scores	Prodrome	Comparison	Comparison
Overall			
BPRS Mean	1.57 (.38)	1.34** (.23)	1.37** (.21)
Factors			
Anxiety-Depression	1.90 (.83)	1.38*** (.44)	
Thought Disturbance	1.57 (.70)	1.12*** (.30)	1.07*** (.21)
Hostile-Suspiciousness	1.44 (.50)	1.22* (.29)	1.12** (.21)
Individual Items			
Somatic Concern	1.82 (1.18)	1.25** (.59)	1.27** (.67)
Depression	2.16 (1.24)	1.37*** (.69)	
Guilt	1.45 (.83)	1.14** (.35)	
Hostility	1.80 (1.00)		1.25** (.56)
Suspiciousness	1.47 (.97)		1.04* (.20)
Unusual Thought Content	2.04 (1.43)	1.33** (.91)	1.18*** (.59)
Grandiosity	1.22 (.58)		1.00** (.00)
Hallucinations	1.80 (1.50)	1.02** (.14)	1.10** (.50)

Note. Numbers in parentheses are standard deviations.

*$p < .10$, compared to the prodromal period, ANOVA period effect

**$p < .05$, compared to the prodromal period, ANOVA period effect

***$p < .01$, compared to the prodromal period, ANOVA period effect

Table 2

ANOVA Period Effect Statistics for BPRS Individual Items

Item	Comparisons	
	Within-Patient	Between-Patient
	Psychotic Prodromes	
Somatic Concern	$F(1, 16) = 5.44$, $p < .04$	$F(1, 32) = 4.96$, $p < .04$
Depression	$F(1, 16) = 14.50$, $p < .002$	
Guilt	$F(1, 16) = 6.90$, $p < .02$	
Hostility		$F(1, 32) = 5.63$, $p < .03$
Suspiciousness		$F(1, 32) = 4.07$, $p < .06$*
Unusual Thought Content	$F(1, 16) = 5.99$, $p < .03$	$F(1, 32) = 10.01$, $p < .004$
Grandiosity		$F(1, 32) = 7.17$, $p < .02$
Hallucinations	$F(1, 16) = 5.62$, $p < .04$	$F(1, 32) = 4.46$, $p < .05$
	Depression/Hostility Prodromes	
Depression	$F(1, 10) = 4.44$, $p < .07$*	
Hostility		$F(1, 20) = 3.29$, $p < .09$*
Tension	$F(1, 10) = 4.23$, $p < .07$*	$F(1, 20) = 9.38$, $p < .007$

*Non-significant tendency.

Table 3

Mean BPRS Scores for Depression/Hostility Prodromes and Comparison Periods

	Six-Week Periods		
		Within-Patient	Between-Patient
BPRS Scores	Prodrome	Comparison	Comparison
Factors			
Activation	1.40 (.48)	1.18** (.28)	1.08** (.17)
Anergia	1.57 (.38)	1.89* (.60)	
Hostile-Suspiciousness	1.37 (.60)		1.11* (.31)
Individual Items			
Depression	2.33 (1.59)	1.55* (.97)	
Hostility	1.41 (.76)		1.15* (.57)
Tension	1.88 (.70)	1.55* (.83)	1.24*** (.50)

Note. Numbers in parentheses are standard deviations.

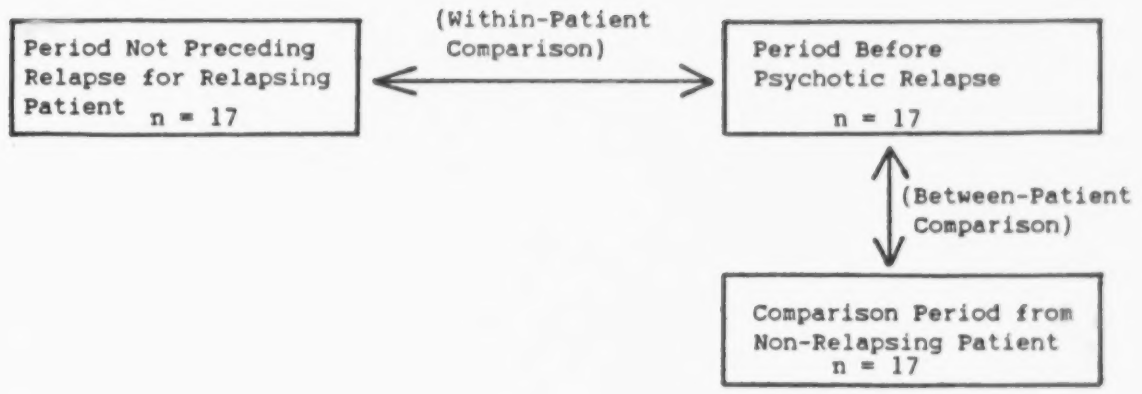
*$p < .10$, compared to the prodromal period, ANOVA period effect

**$p < .05$, compared to the prodromal period, ANOVA period effect

***$p < .01$, compared to the prodromal period, ANOVA period effect

Figure Captions

Figure 1. Overview of research design.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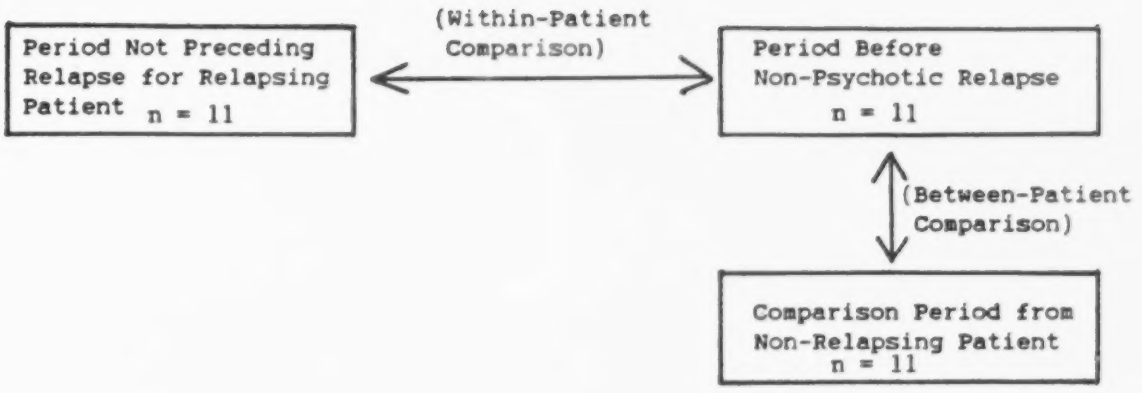
(Within-Patient Comparison)
Period Before Psychotic Relapse n = 17
(Between-Patient Comparison)
Comparison Period from Non-Relapsing Patient n = 17


Period Not Preceding Relapse for Relapsing Patient n = 11
(Within-Patient Comparison)
Period Before Non-Psychotic Relapse n = 11
(Between-Patient Comparison)
Comparison Period from Non-Relapsing Patient n = 11